Amendments to the Claims

1-19 (Canceled)

20. (Currently amended) A ~~plasmid having a~~ nucleic acid moleculesequence ~~region~~ comprising an open reading frame encoding a cleavable single-chain polypeptide, said open reading frame comprising:

a) a first nucleotide sequence ~~region comprising~~ encoding at least a portion of a clostridial neurotoxin heavy chain binding element able to preferentially interact with a target cell surface marker under physiological conditions;

~~i) a first portion encoding a first amino acid sequence region comprising a binding element able to specifically bind a target cell surface marker under physiological conditions; and~~

b) a second nucleotide sequence encoding at least a portion of a clostridial neurotoxin heavy chain translocation element able to facilitate the transfer of said single-chain polypeptide across a vesicular membrane;

~~ii) a second portion encoding a second amino acid sequence region comprising a translocation element able to facilitate the transfer of a polypeptide across a vesicular membrane;~~

[[b]]c) a ~~second~~third nucleotide sequence ~~region~~ encoding ~~a third amino acid sequence region comprising~~at least a portion of a therapeutic element peptide having biological activity when released into the cytoplasm of the target cell, and

d) a fourth nucleotide sequence encoding a peptide comprising a non-native Clostridial neurotoxin protease cleavage site;

wherein said fourth nucleotide sequence intervenes between said second sequence and said third nucleotide sequence.

~~wherein said first and second nucleotide sequence regions are separated by a third nucleotide sequence region encoding a fourth amino acid sequence comprising a protease cleavage site which is cleaved when exposed to a protease, provided said third amino acid sequence region is not cleaved by a human protease or a protease normally expressed by a cell expressing said single-chain polypeptide, and wherein said single-chain polypeptide is expressed by said plasmid within a suitable host cell.~~

21. (Currently amended) The ~~plasmid~~molecule of claim [[20]]20, wherein said ~~first or second nucleotide sequence region~~open reading frame further comprises a fifth nucleotide sequence encoding ~~encodes an amino acid sequence region~~a peptide comprising a target-binding portion of a binding tag.

22. (Currently amended) The ~~plasmid~~molecule of claim [[21]]21, wherein said ~~binding tag comprises a~~ target-binding portion ~~of a polypeptide selected from the group consisting~~

~~of~~comprises a His_6, a monoclonal ~~antibodies~~antibody, a maltose binding protein, a glutathione-S-transferase, a protein A, ~~and~~or a calmodulin binding protein.

23. (Currently amended) The ~~plasmid~~molecule of claim [[20]]20, wherein said ~~first nucleotide sequence region encodes at least a portion of~~binding element is a *Clostridium botulinum* neurotoxin heavy chain ~~a clostridial neurotoxin heavy chain~~.

24. (Currently amended) The ~~plasmid~~molecule of claim [[23]]20, wherein said ~~first nucleotide sequence region encodes at least a portion of~~translocation element is a *Clostridium botulinum* neurotoxin heavy chain.

25. (Currently amended) The ~~plasmid~~molecule of claim [[23]]20, wherein said ~~first nucleotide sequence region encodes at least a portion of~~translocation element is a *Clostridium tetani* neurotoxin heavy chain.

26. (Currently amended) The ~~plasmid~~molecule of ~~either of~~ claim ~~20 or 23~~20, wherein said ~~second nucleotide sequence region encodes at least a portion of~~therapeutic element peptide comprises a clostridial neurotoxin light chain.

27. (Currently amended) The ~~plasmid~~molecule of claim [[26]]26, wherein said ~~second nucleotide sequence region encodes at least a portion of~~clostridial neurotoxin light chain is a *Clostridium botulinum* neurotoxin light chain.

28. (Currently amended) The ~~plasmid~~molecule of claim [[26]]26, wherein said ~~second nucleotide sequence region encodes at least a portion of~~clostridial neurotoxin light chain is a *Clostridium tetani* neurotoxin light chain.

29-31. (Canceled)

32. (Currently amended) A method of making a cleavable single-chain polypeptide ~~derived from a clostridial neurotoxin~~ comprising:

a) inserting the plasmid of any one of claims ~~20-25 or 29-31~~20-28, 31 or 38 into a suitable host cell,
b) growing said host cell in culture, and
c) permitting or inducing the host cell to express the single chain polypeptide encoded by said plasmid.

33. (Currently amended) A method of purifying a ~~recombinant~~cleavable single chain polypeptide ~~derived from a clostridial neurotoxin~~ comprising:

a) lysing a host cell expressing a single chain polypeptide from the plasmid of either of claim 21 or 22 to produce a cell lysate,
b) contacting said cell lysate with a target compound so as to form a specific binding complex capable of being immobilized comprising said binding tag and said target compound, and
c.) separating said binding complex from said cell lysate.

34-37. (Canceled)

38. (New) The molecule of claim 20, wherein said binding element is a *Clostridium tetani* neurotoxin heavy chain.

39. (New) The molecule of claim 20, wherein said protease cleavage site comprising SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 22 or SEQ ID NO: 23.

40. (New) A nucleic acid molecule comprising an open reading frame encoding a cleavable single-chain polypeptide, said open reading frame comprising:

    a) a first nucleotide sequence encoding at least a portion of a binding element peptide able to preferentially interact with a sensory afferent neuron cell surface marker under physiological conditions;

    b) a second nucleotide sequence encoding at least a portion of a clostridial neurotoxin heavy chain translocation element able to facilitate the transfer of said single-chain polypeptide across a vesicular membrane;

    c) a third nucleotide sequence encoding at least a portion of a clostridial neurotoxin light chain therapeutic element having biological activity when released into the cytoplasm of said target cell; and

    d) a fourth nucleotide sequence encoding a peptide comprising a non-native Clostridial neurotoxin protease cleavage site;

    wherein said fourth nucleotide sequence intervenes between said second sequence and said third nucleotide sequence.

41. (New) The molecule of claim 40, wherein said open reading frame further comprises a fifth nucleotide sequence encoding a peptide comprising a target-binding portion of a binding tag.

42. (New) The molecule of claim 41, wherein said target-binding portion comprises a His_6, a monoclonal antibody, a maltose binding protein, a glutathione-S-transferase, a protein A or a calmodulin binding protein.

43. (New) The molecule of claim 40, wherein said translocation element is a *Clostridium botulinum* neurotoxin heavy chain.

44. (New) The molecule of claim 40, wherein said translocation element is a *Clostridium tetani* neurotoxin heavy chain.

45. (New) The molecule of claim 40, wherein said therapeutic element is a *Clostridium botulinum* neurotoxin light chain.

46. (New) The molecule of claim 40, wherein said therapeutic element is a *Clostridium tetani* neurotoxin light chain.

47. (New) The molecule of claim 40, wherein said protease cleavage site comprising SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 22 or SEQ ID NO: 23.